Vascular remodeling of the vitelline artery initiates extravascular emergence of hematopoietic clusters.

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Public Summary:
The origin of blood cells during development has been under significant debate for a number of years. Using genetic techniques, we found that cells that line the inner side of blood vessels (called endothelial cells) are responsible for giving rise to blood cells early during development. In this paper we found that in particular one artery, the vitelline artery produces a large number of blood cells during a short period of embryonic growth. More importantly, the endothelial cells in the vitelline artery as well as other endothelial cells that give rise to blood, are originated by a particular type of tissue called the lateral plate mesoderm. These findings are important because they teach us the basic elements and history required for cells to generate blood. The information will be essential to reproduce these conditions in vitro and generate blood from specific individuals when necessary.

Scientific Abstract:
The vitelline artery is a temporary structure that undergoes extensive remodeling during midgestation to eventually become the superior mesenteric artery (also called the cranial mesenteric artery, in the mouse). Here we show that, during this remodeling process, large clusters of hematopoietic progenitors emerge via extravascular budding and form structures that resemble previously described mesenteric blood islands. We demonstrate through fate mapping of vascular endothelium that these mesenteric blood islands are derived from the endothelium of the vitelline artery. We further show that the vitelline arterial endothelium and subsequent blood island structures originate from a lateral plate mesodermal population. Lineage tracing of the lateral plate mesoderm demonstrates contribution to all hemogenic vascular beds in the embryo, and eventually, all hematopoietic cells in the adult. The intraembryonic hematopoietic cell clusters contain viable, proliferative cells that exhibit hematopoietic stem cell markers and are able to further differentiate into myeloid and erythroid lineages. Vitelline artery-derived hematopoietic progenitor clusters appear between embryonic day 10 and embryonic day 10.75 in the caudal half of the midgut mesentery, but by embryonic day 11.0 are sporadically found on the cranial side of the midgut, thus suggesting possible extravascular migration aided by midgut rotation.